GENENT.091NP PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Vanessa Hsei, et al.	Group Art Unit 1642
Appl. No.	:	09/335,014	
Filed	:	September 13, 1999	
For	:	ANTIBODY FRAGMENT-POLYMER CONJUGATES AND HUMANIZED ANTI-IL-8 MONOCLONAL ANTIBODIES	
Examiner	:	L. Helms	

I hereby certify that this correspondence and all marked attachments are being deposited with the United States Postal Service as first-class mail in an envelope addressed to: United States Patent and Trademark Office, P.O. Box 2327, Arlington, VA 22202, on

June 11, 2002
(Date)

Ginger R. Dreger, Reg. No. 33,055

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COMMUNICATION

United States Patent and Trademark Office
P.O. Box 2327
Arlington, VA 22202

Dear Sir:

The present Communication is filed concurrently with the filing of a Request for Continued Examination of the above-identified patent application. The application was prosecution until final rejection of claims 1-34 in an Office Action mailed December 19, 2001. In an Amendment and Response to Final Office Action mailed on January 11, 2002, applicants requested the cancellation of claims 5 and 14, and the amendment of claims 1 and 6. According to the Advisory Action mailed May 3, 2002, the reply filed on January 11, 2002 did not place the application in condition for allowance, and the rejection of claims 1-34 has been maintained.

Applicants hereby request the entry of the amendments requested in the submission of January 11, 2002, and consideration of the following additional arguments.

ARGUMENTS

In the Advisory Action, the Examiner notes that contrary to applicants' arguments, Faanes et al. teaches antibody fragments. He further states that, in view of Zapata's teaching that "a 10 Kd PEG worked better than the 5Kd PEG, . . . it would be obvious to use a higher MW PEG,"

such as the 40kD species of Faanes et al., and expect the clearance to be further reduced. The Examiner further notes that by using the higher molecular weight PEG, "as Faanes teaches," the apparent size of the conjugate is increased accordingly, thus leading to at least 8-25 fold greater apparent size compared to the antibody fragment, as recited in the claims.

Applicants maintain that the combination of the disclosures of Faanes et al. and Zapata et al., as relied on in the pending rejections, is legally improper.

Although Faanes *et al.* describe the use of both 5 kD and 40 kD PEG molecules for covalent modification of antibodies, and state that one of their goals with such modifications is to increase the serum half life of the antibodies (see, e.g. Abstract), they refer to the 5 kD molecule as being "preferred." See, e.g. column 12, lines 57-59: "*Activated monomethoxypoly(ethylene) glycol (mPEG) of molecular weight 5kD is the most preferred agent for modifying the antibodies of the present invention.*" Accordingly, Faanes *et al.* teach that covalent modification of an antibody with a **lower molecular weight** PEG is more **preferred** for extending serum half life than modification with a higher molecular weight PEG.

In contrast, Zapata *et al.*, based on experiments with a Fab fragment modified by covalent linkage of two different PEG molecules, teach that covalent modification of an antibody fragment with a **higher molecular weight PEG** is more **preferred** for extending serum half life than modification with a lower molecular weight PEG.

Since Faanes *et al.* and Zapata *et al.* have exactly opposite teachings, their combination is clearly improper. It is well established that references that teach away cannot serve to create a *prima facie* case of obviousness. In re Gurley, 27 F.3d 551, 553; 31 USPQ2d 1130, 1132 (Fed. Cir. 1994). If references taken in combination would produce a "seemingly inoperative device," such references teach away from the combination and thus cannot serve as predicates for a *prima facie* case of obviousness. In re Sponnobie, 405 F.2d 578, 587; 160 USPQ237, 244 (CCPA 1969); see also In re Gordon, 733 F.2d 900, 902, 221 USPQ 1125, 1127 (Fed. Cir. 1984). Faanes *et al.* teaches to use lower molecular weight PEG molecules in order to achieve a greater increase in serum half-life. Zapata *et al.* teach to use higher molecular weight PEG molecules in order to achieve a greater increase in serum half life. In other words, Faanes *et al.* teach away from the teaching of Zapata *et al.*, and Zapata *et al.* teach away from the teaching of Faanes *et al.* Since it is impossible to follow both of these opposite teachings simultaneously, the combination would result in a "seemingly inoperative device," and is, therefore, legally improper.

INFORMATION DISCLOSURE STATEMENT

According to the Advisory Action, "there is no 1449 in this case for references which were stated to be provided in 09/121,952," and "09/121,952 was unavailable for inspection." According to applicants' records, in the present case a 1449 form with 109 references was mailed to the Patent Office on March 8, 2001. According to the date stamp appearing on the return receipt postcard, a copy of which is attached, these documents were received in the Patent Office on March 19, 2001. A further copy of the 1449 form is enclosed for the Examiner's convenience. These are the same references that were resubmitted in connection with Serial No. 09/121,952. In view of the large volume of references, which had already been submitted twice, applicants would hope that it will not be necessary to provide a further set of references in the present case. However, if the Examiner continues to have no access to the file of 09/121,952, applicants are ready to submit a further set of reference for the Examiner's consideration.

It is believed that all claims are in *prima facie* condition for allowance, and an early issuance of a Notice of Allowance is respectfully solicited.

Should the Examiner find that there are any further issues outstanding, he is respectfully invited to contact the undersigned attorney in order to arrange a telephone interview.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: _____ By: _____

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